

## Review

# An Overview of Secondary Metabolites of Mango (*Mangifera Indica*) Fruit

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## Abstract

Mango fruit a rich source of various macro and micro-nutrients, fulfilling the dietary requirements of consumers. It has reported to possess numerous polyphenolic secondary metabolites. Major mango polyphenols identified in terms of respective free-radical scavenging ability and concentration in fruit, are mangiferin, quercetin, kaempferol, catechins, rhamnetin, anthocyanins, methyl gallate, gallic acid, ellagic acids, benzoic acid, and protocatechuic acid.

Keywords: Fruit metabolites; Bioactive metabolites; metabolome; Horticulture; mango fruit

## Introduction

Macronutrients such as carbohydrates, lipid and fatty acids, organic acids protein, amino acids micronutrients minerals (potassium and calcium, iron, zinc, copper, magnesium, phosphorus, potassium, sodium, manganese, and selenium) vitamins (vitamin C and vitamin A) and non-nutrients compound (chlorophyll, carotenoids, phenolic compounds flavonoids and volatile compounds) are present in mango fruit [1]. Asian cultivars also presented low contents of total protein (0.5–1%). The energy value associated to 100 g of the pulp of fruit is 60 to 190 kcal (250–795 kJ), making it an important fruit for the human diet. Several pre-harvest and postharvest factors contribute to variation of nutritional, non-nutritional, and water contents of mango fruit [2]. The amino acid composition is found to be varied depending upon cultivars and maturation levels of fruit. The amino acids detected in considerable amounts in ripe state are alanine, serine, leucine, arginine, glycine, and isoleucine, while all other amino acids are present in trace amount [3].

## Vitamins in Mango

Mango fruit mainly has Vitamin C and vitamin A, which suggests that regular

consumption of fruit can fulfil the necessary dietary requirements. Significant variations have been found in vitamin C content that fluctuates from 9.79 to 186 mg/100 g of mango pulp. Vitamin C decreases between 5 to 7 weeks after fruit ripening and storage at room temperature. Which is believed to be due to the involvement of metabolic pathways such as ethylene, oxalate, and tartrate biosynthesis where vitamin C serves as coenzyme of their respective enzymes [4]. The content of vitamin A, despite been prominent contributor to vitamin content of fruit, is found to be varying from 1,000 to 6,000 IU. Usually low or moderate levels of vitamin E are observed in fruit and can occur as tocopherols  $\alpha$ -,  $\beta$ -,  $\lambda$ -, and  $\gamma$ -T. Tocotrienols corresponding tocopherols are  $\alpha$ -,  $\beta$ -,  $\lambda$ -, and  $\gamma$ -T3. The only biologically active form is found to be  $\alpha$ -tocopherol. The E and K vitamins are found only in minor quantities, while vitamin D has not yet detected in fruit by any cultivars so far [5].

## Carbohydrates in Mango

Ripened mango fruit serves as a source of sugars such as glucose, sucrose, and fructose. Starch and pectins are other carbohydrates commonly found in mango fruit. Mango carbohydrates are significant for a nutritional

value of fruit and its flavor. The fruit pulp of ripe mango has found to contain about 15% of total sugars. Fructose serves as major monosaccharide during the pre-maturation phase of fruit. Sucrose, on other hand, is the principal sugar in ripe mango fruit. During stage of ripening, starch hydrolyzes to glucose [6]. Futile cycle is fueled when glucose after phosphorylation enters the hexose phosphate pool, sucrose synthesis and degradation that controls the content of other sugars is regulated. Pectin, an important gelling sugar, is a structural carbohydrate which is abundant in mango pulp. Pectin accumulates in unripe fruit, but its molecular weight decreases when ripening begins [7].

### **Lipids in Mango**

Mango seed and peel are considered to be a source of fatty acids whereas mango pulp only have small quantities of lipids in it. Mango fatty acids as by-products have been used by pharmaceutical and food industries. Fatty acids found prominently in fruit are palmitic, stearic, linoleic, and oleic acid. Fatty acids such as Lignoceric, arachidic, linolenic, and behenic acids are in comparably lower concentrations [8]. The triglycerides content of fruit seeds has found to a blend of 11% to 38.8% of 1,3-dipalmitoyl-2-oleoyl-glycerol (POP), 22.1% to 36.9% of 1,3-distearoyl-2-oleoyl-glycerol (SOS), and 15.4% to 16.2% of 1-palmitoyl-3-stearoyl-2-oleoyl-glycerol (POS). studies on different varieties of mangoes have revealed fatty acid content ranging from 0.75% to 1.7% in fruit peel and 0.8% to 1.36 in fruit pulp where triglycerides are major components of later, while diglycerides and monoglycerides are minor contributors [9].

### **Major Phytochemicals in *Mangifera indica* L (Mango)**

Mango phytochemical imparts the fruit its characteristic color and flavor also making it a rich source of such compounds. Mainly

phenolic compounds are major phytochemicals of mango plant present in various parts such as fruit, kernel (stone), leaves, and bark. The chemical composition of mango fruit and plant altogether is not independent of location of cultivation, variety, and stage of maturity. Carotenoids, the natural organic pigment in plant, imparts characteristic bright yellow color to fruit flesh and peel. Literature reports that carotenoids in fruit are indigenously biosynthesized and their concentration rises upon initiation of ripening stage. Main carotenoids contributors *M. indica* fruit flesh and peel are  $\beta$ -carotene, neoxanthin, zeaxanthin, luteoxanthin, violaxanthin, and cryptoxanthin while  $\beta$ -carotene is the most abundant of all [10]. Terpenoids, a terpene similar class of lipids the imparts aroma to the fruit, is also found to be present in mango plant. Major mango terpenoids, includes careen, ocimene, terpinolene and myrcene. Gallotannins, the hydrolyzable tannins are another class of phytochemicals present in various parts of plant such as bark, leaves, kernel, and fruit flesh. Tocopherol in alpha, beta and gamma –tocopherol form are also reported to be present in fruit peel and flesh [11].

### **Mango Fruit Pulp**

Pulp, which is a major product of mango fruit mangoes, is rich source of various classes of phytochemicals. Mango pulp is found to be containing mangiferin, gallic acids, isoquercetin, ellagic, gallotannins, quercetin, acid, and  $\beta$ -glucogallin polyphenolic compounds. Phenolic acids such as gallic acid, 3,4-dihydroxybenzoic acid, benzoic acid and benzoic acid propyl ester have also been reported in pulp [12]. Phenolic acids are not only in form of gallic acid but also other phenolic acids which are derived from the oxidation of galloyl residues in ellagitannins are present in mango pulp. Triterpenes and triterpenoids class of phytochemicals found

in pulp include cycloartenol, 3 $\beta$ -hydroxycycloart-24-en-26-al, 24-methylene-cycloartan-3 $\beta$ ,26-diol,  $\alpha$ -amyrin,  $\beta$ -amyrin, ocotillol, dammarenediol II, and psi-taraxastane-3 $\beta$ . Resorcinolic lipids such as heptadecenyl-resorcinol and heptadecadienyl)-resorcinol have also been identified in mango pulp. Carotenoids include  $\beta$ -carotene, cis-violaxanthin, neochrome, cis-neoxanthin, luteoxanthin and zeaxanthin are known to give pulp its characteristic color [13].

### **Mango Fruit Peel**

Major by-product of mango processing industry is mango peel and constitutes about 15–20% of total weight of the fruit. Peel has been found to be a rich source of polyphenols, dietary fiber, vitamin E, carotenoids and vitamin C. Among polyphenolic class of phytochemicals mango peel has found to contain mangiferin, quercetin, ellagic acid, kaempferol, rhamnetin, and their related conjugates. Acetone extract of mango peel provides with acids such as gallic, protocatechuic, gentisic, and syringic acids as in bound states [14]. Carotenoids and anthocyanins contents mango peel are relatively high in ripe fruit, whereas polyphenols are major constituent of unripe fruit peel. Flavonol, xanthone C-glycosides, gallotannins, and benzophenone derivatives are found to be abundant in peel than any other plant part. So far 18 gallotannins and 5 benzophenone derivatives have been detected in mango peel, which are assumingly characterized as galloylatedmaclurin and iriflophenone glucosides [15].

### **Mango Kernel (Stone of Mango)**

Phenolic compounds including microelements such as selenium, copper, and zinc can be obtained in good enough quantity from mango kernel or stone. Studies have shown that antioxidant effect of the mango

kernel are attributed to high content of sesquiterpenoids, phytosterols, and microelements in it [16]. Commonly found polyphenols in kernel are tannin, coumarin, caffeic acid, vanillin, gallic acid, mangiferin, ferulic acid, cinnamic acid. Long-chain hydrocarbons and fatty acids reported in mango kernel includes stearic acid, linolenic, oleic acid, arachidonic acid, eicosanoic acid and palmitic acid. Sterols that are found in kernel include stigmasterol, campesterol and sitosterol [17]. Triterpenes and triterpenoids class of phytochemicals in mango kernel include limonene,  $\alpha$ -pinene,  $\beta$ -pinene and myrcene. Phenolic acids such as ascorbic acid, quercetin, and gallic acid are also found in mango kernel [18].

### **Mango Plant Leaf and bark**

Mango leaves and bark are found of containing very high levels of phenolic compounds than any other plant part, making them capable of potential pharmaceutical activities. Mangiferin (C-2- $\beta$ -D-glucopyranosyl-1,3,6,7-tetrahydroxyxanthone) was first identified and isolated from mango leaves, while homomangiferin (1,6,7-trihydroxy-3-methoxy-2-C- $\beta$ -D-glucopyranosyl-xanthone) is reported to be first is isolated from bark [19]. Identified phytochemicals of mango bark includes protocatechuic acid, alanine, glycine, catechin, mangiferin,  $\gamma$ -amino-butyric acid, kinic acid, shikimic acid, and the tetra cyclic triterpenoid. Significant amounts of polyphenols are present in mango leaves such as mangiferin, xanthonoids, and gallic acid. In addition, the mangiferin, one toxic compound has been identified and isolated from mango leaves of Alphonso mangoes called pyrogallol (1,2,3-Trihydroxybenzene. The presence of mangiferin as a main component of the mango bark extract is so much recognized that is now commercially available in Brazil under the name of Vimang [20].

### Major polyphenols of Mango (*Mangifera indica* L.)

Polyphenols are secondary metabolites of plants which are found discriminately distributed in beverages and plant-processed foods. Studies indicate that 1 g of total polyphenols is frequently consumed by healthy individuals per day which have not found to cause any acute or lethal toxicity. Phenolic compounds have intrinsic capability to decrease lipid peroxidation and prevent oxidative damage to DNA through free radical scavenging action [21]. Free radicals are established cause of change in gene expression, and induction of abnormal proteins which in turn leads to degenerative diseases and aging. Polyphenols are also known to prevent events leading to degenerative diseases such as inhibition of cellular communication [22].

Polyphenols are categorized on basis of their respective carbon structure and arrangement according to which main classes of polyphenols are phenolic acids, flavonoids, lignans and stilbenes. Literature also reports existence of other types of polyphenols which are not well defined or have been found to be produced from oxidative polymerization of phenolic acids and flavonoids. Polyphenol extraction from plants have reported to be ne crucial step as compound denaturation by heat or lost due to solvent are common issues [12]. Besides this reason, toxic nature of some solvents makes it more difficult to obtain polyphenols from plant source safely. Decoction so far seems to be the extraction method of choice which is also adopted and applied to industrial polyphenolic production from mango bark. Techniques applied from specific polyphenolic determination and quantification commonly are chromatographic coupled with mass spectrometry or reduction reactions with Folin-Ciocalteu reagent. Anti-oxidative

assays of plant extracts are utilized to predict and estimate polyphenolic content and activity capacity [23].

### Mangiferin

Mangiferin belongs to xanthone class of phytochemicals which are one of most potent antioxidants reported in literature. Xanthones through experimentations have established to be more potent than both vitamin C and vitamin E which had gained them unofficial title of “super antioxidants”. Xanthones are known to be heatstable molecules. Mangiferin is also called C-glucosyl xanthone, is found to be widely distributed in higher plants providing protection to plants against different dynamic stresses including attack of pathogenic microorganisms [24]. It is present as a biological polyphenolic antioxidant in the bark, roots, fruit and leaves of *Mangifera indica* Linn, making the plant potential option for mitigating a number of immune-deficiency diseases [25].

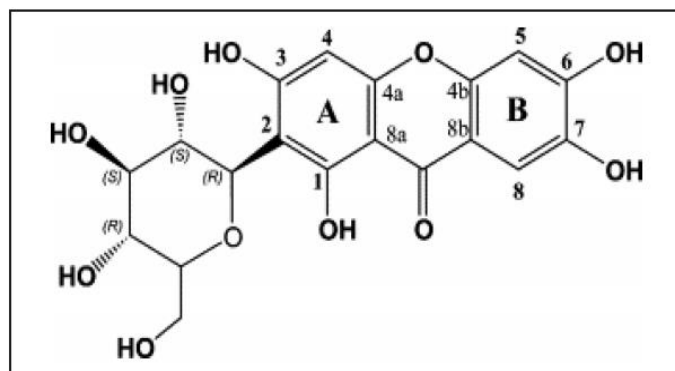


Figure 1: Chemical structure of mangiferin [12]

### Biological Benefits of Mangiferin

It has been established through experimentation that mangiferin acts as active principle phytochemical of mango stem, pulp and leaf extract to contribute to biological activities of extracts. Various studies have reported a wide range of pharmacological effects of mangiferin from different parts of plant. Potential biological activities include antioxidant, anti-allergenic,

anti-inflammatory, analgesic, anticancer, antimicrobial, antiatherosclerotic, and immunomodulatory action [26]. In an investigation of in vitro antiviral and immune-stimulatory actions of mangiferin, it showed to protect hepatocytes, neutrophils, lymphocytes, and macrophages from static oxidative stress which contributed to reduce atherogenicity in streptozotocin model of diabetic rats; and also prevented rats against oxidative damage renal and cardiac tissues in streptozotocin-induced oxidative stress models [27]. Experiments have predicted a potential possible mechanism to explain bioactivities of mangiferin according to which mangiferin mainly has ability to function as an antioxidant and radical captodative agent. A biologically active mangiferin even at low concentration, compared to those of target substrates for oxidation such as membrane lipid or DNA, significantly delays or protect against oxidative damage [28].

Mangiferin works at different levels in oxidation sequence to inhibit it in case of lipid peroxidation it provides protection from oxidation by decreasing O<sub>2</sub> concentration and forming mangiferin phenoxy radicals. It also binds to metal ions such as (Fe<sup>2+/3+</sup>) forming a mangiferin-iron complex which is a stable and a complex structure that does not allow further generation of damaging radicals [29].

### **Flavonoids**

Flavonoids, which were once believed to be vitamins, now are separate class polyphenolic phytochemicals which are most abundant type of polyphenol in human diet. Flavonoids are further categorized on basis of oxygen heterocycle degree of oxidation according to which classes are flavones, isoflavones, flavonols, flavanols, flavanones, anthocyanins and proanthocyanidins. The occurrence of some of these flavonoids is limited to only few foodstuffs. Quercetin, the

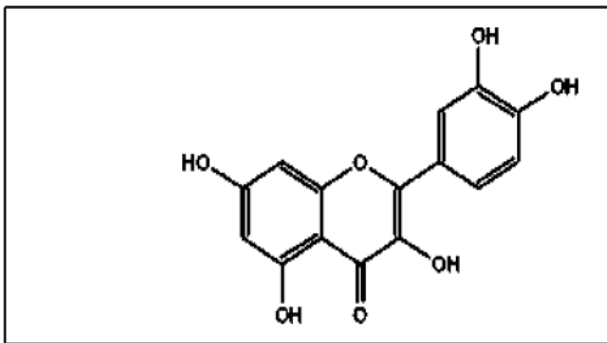
major flavonol present in daily diet, is widely distributed in fruits and vegetables, while other flavones occur rarely and present in a sugar bound state as O-glycosides. Flavonoids possessing diphenylpropane skeleton are believed to have antioxidative, anticarcinogenic, anti-inflammatory, antimutagenic, antiallergic biological properties [30]. The flavonoids reported to be commonly present in mango include catechin, quercetin, isoquercetin (quercetin-3-glucoside), epicatechin, fisetin, and astragalin (kaempferol-3-glucoside). The flavonoid glucosides are reported to have frequent occurrence in mango leaves, whereas fisetin is rare in leaves. Quercetin is present in unripe mango fruits in high quantiles but tend to disappear on ripening. The peel of mango varieties from few cultivators have showed presence of peonidin-3-galactoside. The reddish tint of few mango varieties have been found to associated to presence anthocyanins, another group of phenolic phytochemicals having antioxidant potentials higher than that of phenolic acids [31].

### **Quercetin**

Quercetins, a class of flavonoids majorly responsible for providing characteristic colors to many fruits, flowers, and vegetables. They often occur in bound states as glycosides, such as rutin. The presence of quercetin and other related glycosides such as quercetin 3-galactoside quantified in mango pulp to be 22.1 mg/kg, quercetin 3-glucoside is reported to be 16.0 mg/kg and quercetin 3-arabinoside has found to be 5.0 mg/kg. The ability of modulating the transactivation of peroxisome proliferator-activated receptors (PPARs) of mango quercetin have been established through gene reporter assay.

Some conjugates of quercetin such as quercetin xylosides, quercetin rhamnosides, and quercetin galactosides have not found to

be hydrolysable by lactase and hydrolase, which makes them un-absorbable through small intestine. In comparison, quercetin glucosides and free quercetin have demonstrated to be hydrolysable through enzymes and hence bioavailable through small intestine [32].



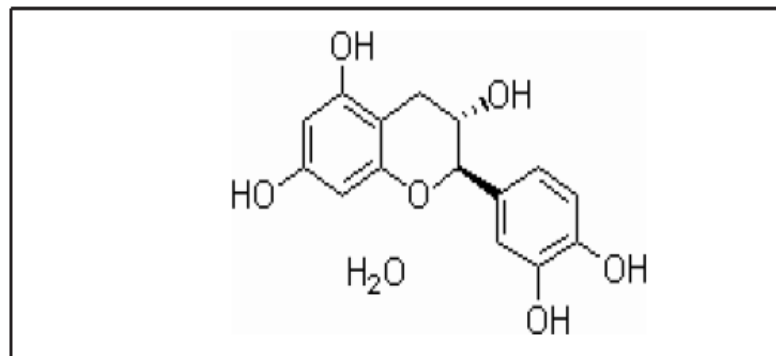
**Figure 2: Chemical structure of Quercetin [12]**

Quercetin has found to downregulate replication of mutant breast cancer cells [33]. It has also exhibited arrests abnormal human leukemic T cells, inhibiting tyrosine kinase and heat shock proteins [34]. Quercetin in some studies have shown to protect Caco-2 (adenocarcinoma cell line) cells from lipid peroxidation and oxidative damage induced by free radicals such as hydrogen peroxide and Fe<sup>2+</sup> [35]. In mouse liver cells, quercetin has shown to increase glutathione, while decreasing lipid oxidative damage, thus protecting the liver from oxidative stress (Molina et.al 2003). In colon carcinoma and in mammary adenocarcinoma cell lines, quercetin has shown to inhibit proliferation [36]. Lower doses of quercetin have surprisingly shown to contribute to enhance cell proliferation in colon and breast cancer cells. Quercetin have presented inhibition of human leukemia cells, through induction of apoptosis [37].

### Catechins

Catechin class of flavanoids present in mango plant includes epicatechin, epicatechingallate, epigallocatechin, and galocatechin. The polyphenolic mango pulp

extract represents 50% of constituents to be catechin, and epicatechin. Catechin together with epicatechin, contributes to 11% polyphenolic mango bark extract. The bioactivity of catechin and epicatechin is attributed to their strong antioxidative given them good medicinal values. Several epidemiological and in vitro studies suggest that catechins have beneficial effects on human health due to their free radical scavenging and antioxidant activities serving to protect against congestive heart failure myoglobinuric acute renal failure, to reduce the incidence of myocardial ischemia, and to support anti-aging [38].



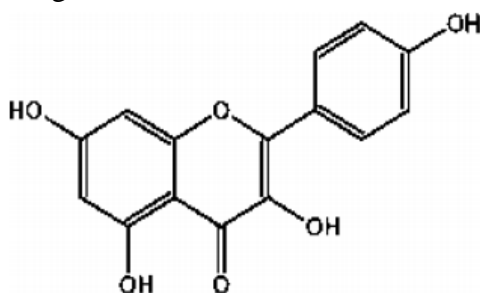
**Figure 3: Chemical structure of catechin [12]**

### Kaempferol, Rhamnetin and Anthocynins

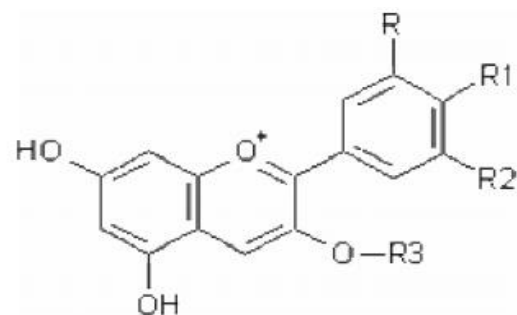
Little information is available about kaempferol class of flavonoids in the mango. Studies have been centered only on the identification and characterization only but little or no experiments detailing its effect on human or animal health are available. Kaempferol and its related conjugates are found existing in almost same quantities in mango pulp. Few in vitro studies have reported antioxidant capacity of kaempferol. Elsewhere the data presents the potential beneficial anti-cancer effect through decrease in cancer cell resistance to inhibiting drugs [39].

Rhamnetin type of flavonoid phytochemical is reported to be present in mango peel in quantity 94.4 mg/kg [40]. Researchers have found cholesterol lowering actions of

rhamnetin in animal model through studies involving effects of pure compound in serum and liver cholesterol levels. In animal models the level of liver oxidases and catalases have shown no effect by intake of rhamnetin [41]. Acceleration of research interest in anthocyanins class of flavanoids is attributed to its potential health benefits as dietary antioxidants. Over 300 structurally different forms of anthocyanins have been identified and characterized in nature. The total anthocyanin content is found to be high in peel of ripe mango ranging from 360 to 565mg/100g, whereas unripe peels contain about 203 to 326mg/100g anthocyanin. In recent past a unique anthocyanin 7-O-methylcyanidin 3-O- $\beta$ -D-galactopyranoside has been found in the mango peel, yet little is known about its biological activities. Anthocyanins have been believed to decrease oxidative stress in diseases such as to exert stress such as coronary heart disease and cancer. It also has shown ability protect against DNA oxidative damage, preventing inflammation and blood vessel disruption. Few researchers have reported potential of anthocyanins to protect against neurodegenerative which can possibly contribute to reverse of age-related neurological deficits in animals [42].



**Figure 4: Chemical structure of kaempferol** [12]



**Figure 5: Chemical structure of anthocyanins** [12]

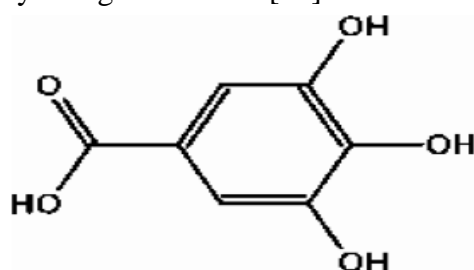
### Phenolic acids

Phenolic acids are found to be present in abundance in plant proceed foods. Among this class of phytochemicals already identified in the mango fruit are gallic acid, gallic acid methyl ester, 3,4-dihydroxybenzoic acid, benzoic acid, gallic acid propyl ester, and benzoic acid propyl ester. Phenolic acids are usually esterified to a polyol, such as glucose. The phenolic acids in form of tannins in mango fruit are either gallic acid derivative; gallotannins (mango fruit) or derived from the oxidation of galloyl residues such as in ellagitannins [32].

### Gallic acid, and its derivatives

Gallic acid is 3, 4, 5-trihydroxybenzoic acid it has found to exist in mango plant exist either in the free form or bound as gallo-tannins. Since the compound has hydroxyl and carboxylic acid group simultaneously present, I structure thus have capability of esterification resulting in formation of digallic acid. Gallic acid does not impart any astringent taste to fruit since it has no affinity to bind to fruit proteins. Gallic acid is identified and characterized as the major polyphenolic phytochemical present in mango fruit, its amount in mango seed extract is found ranging from 23 to 838 mg/100 g in dry matter [43]. Mango stem bark extract has reported the total content of gallic acid to be 226.2 mg/100g in dry matter. 6.9 mg/kg of gallic acid has been quantified in mango pulp, making it major phenolic acid of fruit pulp. Gallic acid generally has reported

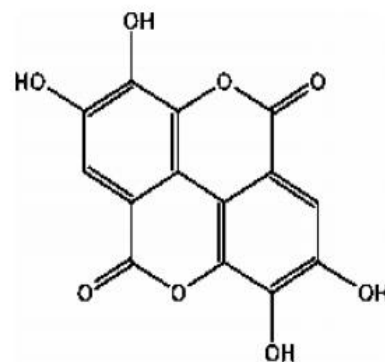
decreasing significantly (about 22%) at stage of initiation of fruit ripening, which is from full green to mature ripe yellow fruit. Levels of gallic acid in fruit have shown to remain unaffected by postharvest invasive pest control treatment, such as washing with hot water [44]. Gallic acid in various studies shown to have anti-inflammatory, antimicrobial, antioxidant, antimutagenic, anticancer and radical scavenging activities. It has shown to decrease histamine release in rat basophilic leukemia cells, inhibiting inflammatory allergic reactions [45].



**Figure 6: Structure of Gallic acid [12]**

### Ellagic acid

Ellagic acid has a structure of a fused 4-ring polyphenol that is widely distributed in mango and other plants. It is found to be present in form of ellagitannin, ellagic acid in a bounded state with sugar molecule making it more water-soluble and hence easy to absorb through intestine. Mango seed extract have shown quantity of ellagic acid to be 3 to 156 mg/100 g in dry matter (Soong et.al). Various studies have shown ability of ellagic acid to inhibit the DNA binding and adduct formation with N-nitrosobenzylmethylamine in cultured tissues of rat esophagus thus producing antimutagenic effects [46]. Ellagic acid have also shown to possess antiviral, antioxidant properties and stimulating the action of detoxifying enzymes. Purified ellagic acid have shown to be less effective and bioavailable than small amounts of ellagitannins from natural sources in human diet [47].

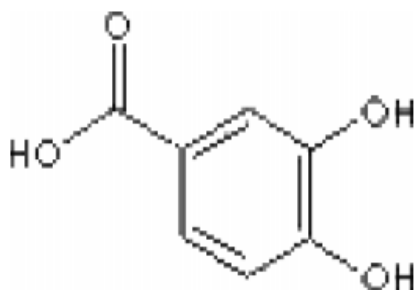


**Figure 7: Chemical structure of Ellagic acid [12]**

### Benzoic acid

Benzoic acid is one of the simplest aromatic carboxylic acids which contains a carboxyl group directly bounded to a benzene ring. It is found to present in mango stem bark extract in quantity of about 198.6 mg/100 g, while the conjugates of benzoic acid such as benzoic acid propyl ester have quantified to be about 398.7 mg/100 g in same extract. Benzoic acid and its polyphenolic derivatives have shown to be principle active ingredient in mango stem bark nutritional supplements. Studies have demonstrated the ability of induction of mitochondrial permeability transition (MPT) in rat liver mitochondria, of mango stem bark benzoic acid. Mango plant stem, beside benzoic acid, also shown to have dihydrobenzoic acids such as Protocatechuic acid which chemically is 3, 4 dihydroxybenzoic acid. This form of dihydroxybenzoic acid has quantified to be about 226.2 mg/100 g of dry matter of stem bark extract. Dihydroxybenzoic acids obtained from mango stem have shown antirheumatic, antipyretic and analgesic biological effects in some studies [48]. Various studies on benzoic acids and its related derivatives have shown its beneficial pharmacological actions such as antifungal, antibacterial, antimutagenic, anticarcinogenic, antioxidant, and neuroprotective [3]. Several other phenolic acids, beside mentioned above, are present in

mango plant in small quantities such as cinnamic acid 11.2 mg/kg, caffeic acid 7.7 mg/kg and ferulic acid 10.4 mg/kg. All these phenolic acids have presented strong antioxidative capabilities which due to their small quantity is negligible from nutraceutical perspective but definitely not irrelevant [12].



**Figure 8: Chemical structure of Protocatechuic acid [12]**

### **Tannins**

Tannins are generally present as phenolic secondary metabolite having water solubility in mango fruit with their in size ranging from 300 to 3000 amu. Tannins based on their structural characteristics are divided in to four classes: gallotannins, ellagitannins, condensed tannins and complex tannins. Phenolic acid derived tannins which are hydrolyzable have limited occurrence as compared to condensed tannins. Tannins shown protein binding resulting in formation of either soluble or insoluble complexes in mango fruit. Gallotannins have been characterized as prominent class of phytochemical in mango pulp with size ranging from 787 – 1243 amu. About 75% of

mango seed extract is found to be composed of hydrolyzable tannins. Tannins have shown to have toxic effects in in-vivo studies that can be reduced by pre-treatment in food processing steps such as water blanching which provides with desired leaching of tannic substances in to soak water while limiting its generation by enzymatic processes [49].

### **Terpenoids**

Terpenoids belongs to the prenyl lipids class of phytochemicals and are found widespread in natural products. Monoterpenes and diterpenes, allopathic agents act as attractant or repellent to regulate plant-herbivorous. Carotenoids belongs to this class of phytochemicals containing contain mono,di and tri terpenoids. Mango terpenoids includes limonene, terpinolene, ocimene, myrcene and careen. Various studies have demonstrated terpenoids to be biologically active in inhibition cell replication and cyclin D1 gene expression in human cancer cell lines. Different mechanism of actions has been proposed through experimentation for chemoprevention action of terpenoids. Synergistic antioxidant capacity of terpenoid combinations of rutin with terpinene have been established through experiments. Presence of such biologically important class of compound with evident human health benefits in mango fruit adds to its functional value in diet [50].

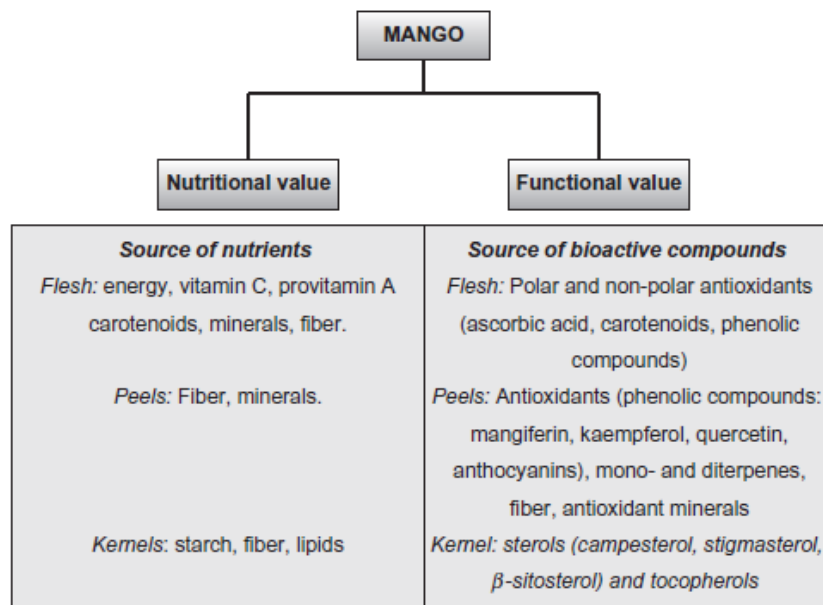


Figure 9: Summary of functional and nutritional components of mango plant [4]

## Health Promoting Benefits of Bioactive Compounds of Mango

### Anti-microbial activity of mango metabolites

Various extracts of roots, fruit peel, leaves, bark and flesh, and kernel of *M. indica* using different solvents systems have been subjected to investigation of antibacterial action. Among various plant parts, mango seed, stone and leaves appear to be thoroughly undertaken for examination of antimicrobial potentials [51]. In a study conducted on mango variety in methanol solvent extraction system, a strong inhibitory effect against *Escherichia coli* was observed. In another study for determining the effect of different solvents on antimicrobial capacity of mango kernel phytochemicals, results indicated strong antibacterial effects of benzene, methanol, hexane, chloroform, and water extracts kernel in inhibiting the growth of *dysenteries* and *Shigella*, with methanolic extract being most potent. Studies have reported antibacterial capacity of aqueous mango kernel extracts of two other *M. indica*

varieties in India. The aqueous extracts were subjected to study of effect against *Pseudomonas aeruginosa* and *Staphylococcus aureus* where they prove to have significant inhibitory action on bacterial growth [52]. Mango kernel extracts having different solvents such as methanol, ethanol, acetone, and phosphate buffer saline have shown to have considerable inhibitory action against growth of *S. aureus*, *P. aeruginosa*, *E. coli* and *Bacillus subtilis*. While the ethanolic and methanolic kernel extract exhibited most potent of all antibacterial capacity against given microbes. Methanolic kernel extract of a *M. indica* variety from inhibitory effect on growth of Japan has shown significant antibacterial action against 43 bacterial species. Efforts have been done to determine antibacterial activity of mango leaves extracts and in a recent study aqueous and chloroform phenolic leaf extracts shown to have inhibitory action on growth *S. aureus*, while extracts with chloroform as solvent being more effective antibacterial [53]. Acetone, methanol and aqueous of leaves of *M. indica* variety from Nigeria have been

successfully tested to have antibacterial potentials against *P. aeruginosa*, *Streptococcus pneumoniae*, *Proteus mirabilis*, *Shigella flexneri*, *E. coli*, *S. aureus*, *Streptococcus pyogenes*, *Bacillus cereus* and *Salmonella typhi*. Extract of leaves of *M. indica* variety from Pakistan have also been investigated to have significant antibacterial action against multidrug resistant *S. typhi*. Gallotannins type of phytochemicals from mango kernel of different varieties have shown to possess antibacterial activity against several pathogens such as *Streptococcus sanguis*, *Streptococcus mutans*, *Streptococcus salivarius* and *Streptococcus mitis*. Inhibitory action of mango tannins is believed to be due to iron complexing properties of compound [54].

#### **Antioxidant activity of mango metabolites**

Several classes of phytochemicals from different parts of mango plant such as phenolic acids, flavonoids and polyphenols have shown to have good free radical scavenging action making them good natural antioxidants. Various pharmacological studies have presented that antioxidant potentials of parts of plants are related to total polyphenolic content of that plant part. In a study conducted in Pakistan to measure Langra and Chaunsa mango variety's antioxidant potentials, significant free radical scavenging was observed. In same study it was also reported that methanolic peel extract of chaunsa and fruit flesh of langra mango have comparable antioxidant effects. Polyphenols such as phenolic acid have capability of donating hydrogen atom to neutralize free radicals while they also possess ability to donate electron for regeneration of other phenols that are natural pro-oxidant. [55]. This regeneration mechanism attributes to Protocatechuic acid and gallic due to their natural structural conformation and high content of hydroxyl groups have shown to have highest

antioxidant capacity of all phenolic acids. Studies have shown that except vanillic acid other phenolic acids in a mixture in extract have positive interaction enabling them to exert synergistic effect possibly because of regeneration mechanism [56].

#### **Antifungal activity of mango metabolites**

Several studies have presented significant antifungal activity of *M. indica* extracts from various plant parts. Ethanolic extracts of leaves of *M. indica* variety in Nigeria have shown to have inhibitory effect on growth of *Pythium aphanidermatum* *Fusarium oxysporum* and *Fusarium avenaceum*. Methanolic leaf extracts on other hand exhibited moderate antifungal effect against *Aspergillus ustus*, *Aspergillus ochraceus* and *Aspergillus niger*. Aqueous leaf extract of *M. indica* variety from Mexico has shown to exert antifungal effect against *Colletotrichum gloeosporioides* strains. Antifungal potentials of flavonoids from mango bark methanolic and ethanolic extracts have also been explored against various pathogenic fungi, yet specific mechanism of action of compounds cannot be stated with certitude [57].

#### **Antitumor activity of mango metabolites**

Many extracts prepared from different parts of mango plant and isolated phytochemicals of various plant parts have shown to exert anticancer effects to counter abnormal cell proliferation. *M. indica* variety from Thailand, Australia and China have shown to have anti-proliferative agents working against HepG2 cells in their peel extracts. *M. indica* ethanolic peel extract have also exhibited the ability of apoptosis induction in HeLa cell lines of human cervical adenocarcinoma, which is investigated to be mainly attributed to induction of expression of apoptotic proteins such as caspases Bax, Bcl-2 and Bid. Antitumor activity of mango phytochemicals has been owed to presence of

quercetin 3-O-galactoside, alpha tocopherol, mangiferin gallate, mangiferin, gallic acid, linoleic acid, kaempferol 3-glucoside and quercetin-3-O-arabinopyranoside in extracts. Cancer protective effects in peel and flesh extract of Korean *M. indica* have been studied and established against HepG2 (human liver cancer cell-line) cells with H<sub>2</sub>O<sub>2</sub>-induced cytotoxicity. Apoptotic effects of mango fruit flesh aqueous extract have been found against colorectal cancer in mouse model and in human colon adenocarcinoma cell line (SW480) [58]. Ethanolic extract of mango seed have exhibited negative effect on cellular proliferation through oxidative stress in human triple negative breast cancer cells (MDA-MB-231). Antitumor effects of mangiferin have been illustrated through various studies against lung, ovary, breast, brain, and cervix cancer cell lines, antiproliferative effects of this bio-active mango xanthonoid is well-documented in literature [59].

#### **Analgesic and anti-inflammatory activity of mango metabolites**

Organic or aqueous extracts from various parts of mango plant have demonstrated to have anti-inflammatory action. Extracts of organic nature from *M. indica* have shown to decrease inflammation in ulcerative colitis animal models. In study on biological beneficial activities of extracts from mango fruit variety of Mexico attenuation of inflammation was observed mainly through expression of anti-inflammatory pathways (PI3K/AKT/mTOR). Mango fruit flesh extracts having high quantity of polyphenols have shown to inhibit inflammatory pathway IGF-1R/AKT/mTOR to mitigate ulcerative colitis. Aqueous stem extract of *M. indica* have shown to reduce inflammation in case of colitis through reduction in TNFR-2, TNF-, COX-2, and iNOS levels in tissue. Mango phytochemicals have shown capacity of

inhibiting tumor necrosis factor alpha (TNF), PGE<sub>2</sub> (prostaglandin E<sub>2</sub>) or LTB<sub>4</sub> (Leukotriene B<sub>4</sub>) in in-vitro studies in stimulus induced inflamed macrophages cells (RAW264.7). Mango fruit extracts have shown to produce significant reduction in nociceptive pain in mice illustrated through acetic acid and hot-plate pain animal models. In another study using acid-induced pain rat models, *M. indica* extracts have shown to reduce writhing response. Formalin-induced licking and abdominal restriction induced through acetic acid was also found to be alleviated by methanolic mango leaf extracts [60].

#### ***Mangifera indica* L. varieties in Pakistan**

Pakistan is known to be the 5<sup>th</sup> largest producer of mango fruit and 3 largest exporters of fruit in the world. Favorable climatic condition enables Pakistan to restore fresh mango supply over a period of 5-6 months making mango the second largest fruit produced by country after citrus. Punjab and Sindh provinces of country documented are largest cultivators of mango with a production capacity of about 300 hectares [61]. Mango is majorly cultivated in early March or month of February, while harvesting months of fruit in country are July and June. Pakistan, with more than 200 mango varieties in nation, still holds Sindhri and Chaunsa its favorite due to rich taste and flavor of fruit. Mango fruit breeding is not much known or established protocol in country generally open pollination is responsible for chance seedling. Tissue culturing and germplasm are relatively new concepts to cultivars. Mango hybrids technologies have been searched to boost industry of mango which faces decline due to high water table, unbalanced fertilization, soil salinity and insufficient plant protection measures. Spread of fungal diseases and destructive pests such as *Drosicha mangiferae* remain to be major threat to

mango plant in country. Farms of Tando Ali in district Badin of Sindh works to suffice national and international needs of fruit exporting its mangoes, mainly Dussehri to to China, Europe, Dubai, and Iran [62].

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